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DOI: https://doi.org/10.1080/00365521.2019.1619826

The relationship between *Helicobacter pylori*–related microbiota dysbiosis and gastrointestinal tract pathologies

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Key words: *Helicobacter pylori*; gastric microbiota; dysbiosis; gastric cancer; esophageal cancer

Conflict of Interest: None declared

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To the Editor,

In their review, Zhang et al. [1], concluded that gastrointestinal microbiota (GI-M) plays an essential role in the development and progression of gastric pathologies; they considered a potential impact of *Helicobacter pylori* infection (*Hp*-I) on gastric microbiota (GM) composition in gastric cancer (GC) pathophysiology, though it remains to be elucidated.

In this regard, apart form the mentioned gastric microbiota influenced by *Hp* colonization, the authors did not take into consideration specific pathogens including species frorm *Campylobacter* genus that appear to be involved in gastric carcinogenesis. *Hp* abundance is positively correlated with the presence of *Campylobacter* which is the most well-connected and influential bacterium observed in *Hp*-related atrophic gastritis patients and could be an substantial contributor to gastric carcinogenesis [2,3].

In this concern, it has been proposed that chronic *Hp*-I induces atrophic gastritis accompanying by decreased acid secretion and acid reflux, thereby reducing the risk of gastroesophageal reflux disease (GERD) and its complications Barrett's esophagus (BE) and esophageal adenocarcinoma (EAC) [4]. However, this conventional consideration might represent a double- edged sword one view. Regarding the opposed view, hypochlorhdria induced by *Hp*-related atrophic gastritis, results in dysbiosis of GI-M, which, beyond GC, could also contribute to BE-EAC sequence [3,5]. Data on BE biofilm show high level of atypical nitrate reducing *Campylobacter* species in BE, compared with non-BE specimens [6] and these species might contribute to development, exacerbation and/or BE progression to EAC through chronic inflammation [5]. Therefore, *Campylobacte*r species and other pathgens-related dysbiosis associated with *Hp*-induced atrophic gastritis might be etiological agents of the chronic esophageal inflammation leading to EAC development [5,7] and thus further investigation is needed.

The authors considered molecular mechanisms involved in *Hp*-I related gastric

cancinogenesis [1]. Likewise, concerning the role of molecular events involved in *Hp*-I-related GERD- BE-EAC sequence, we recently summarized [8] comparable *Hp*-related mechanisms such as the following: *Hp* induction of upper and lower gastrointestinal tract (GIT) oncogenic gastrin, which stimulates proliferation via Janus Kinase (JAK) 2 and Akt-dependent nuclear factor-kappa B (NF-κB) activation in Barrett's EAC cells, displays a anti-apoptotic effect through Bcl-2 protein and survivin upregulations, and induces the mitogenic and oncogenic cyclooxygenase (COX)-2 expression. *Hp* activates the mentioned NF-κB, a transcription regulator of inflammatory genes, including COX-2 that regulates gastrointestinal neoplasm cell growth and proliferation. Prostaglandins (PGs) derived from upregulated COX-2 contribute to BE cancer progression, by perpetuating chronic inflammation and the mitogenic and antiapoptotic effects of PGs are mediated through activation of several aforementioned signaling pathways including NF-κB**,** Src, JAK2/STAT3, ERK, MAPK and PI3K/Akt kinases. Moreover, *Hp*-I could induce specific molecular changes (genetic instability, E-cadherin methylation, monoclonal antibody Das-1) linked with BE pathophysiology, and promotes Ki-67 expression predicting malignant progression in BE. Finally, *Hp*-related metabolic syndrome (MetS) disorders that associated with GI-M dysbiosis appear to be involved in gastric and esophageal carcinogenesis [9,10]. Again, we recently reviewed several *Hp*-related MetS mechanisms involved in upper and lower GIT oncogenic processes [9].

Therefore, *Hp* eradication and manipulation of its related GI-M dysbiosis might inhibit the aforementioned GIT oncogenic processes, and thus further studies are necessary.

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